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☐ 1: Curr Med Chem. 2001 Nov;8(13):1605-48.

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Peptide-binding G protein-coupled receptors: new opportunities for drug design.

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Over the last decades distinct members of the G Protein-Coupled Receptor (GPCR) family emerged as prominent drug targets within pharmaceutical research, since approximately 60 % of marketed prescription drugs act by selectively addressing representatives of that class of transmembrane signal transduction systems. It is noteworthy that the majority of GPCR-targeted drugs elicit their biological activity by selective agonism or antagonism of biogenic monoamine receptors, while the development status of peptide-binding GPCR-addressing compounds is still in its infancy. Exemplified on selected medicinal chemistry projects, this review will focus on the opportunities of therapeutic intervention into a broad spectrum of disease processes through agonizing or antagonizing the functions of peptide-binding GPCRs. In this context, a brief overview of GPCR-mediated signal transduction pathways will be given in order to emphasize the biomedical relevance of a controlled modulation of receptor function. Modern trends on lead finding and optimization strategies for peptide-binding GPCR-targeted low-molecular weight compounds will be highlighted on the basis of current research programs conducted in the areas of angiotensin II, endothelin, bradykinin, neurokinin, neuropeptide Y, LHRH, C5a antagonists, and somatostatin agonists, respectively. Special emphasis will be laid on the elaboration and utilization of structural rationales on the potential drug candidates, thus facilitating more detailed insights into the underlying molecular recognition event.

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